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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/686,783	10/24/00	LANGLETIN M	GEI-078

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EXAMINER	
HUI,S	

ART UNIT	PAPER NUMBER
1617	10

DATE MAILED: 10/23/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application N .	Applicant(s)	
	09/646,763	LANQUETIN ET AL.	
	Examin r	Art Unit	
	San-ming Hui	1617	

-- The MAILING DATE of this communication appears on the cover she t with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 August 2001* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3 and 5-18* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3 and 5-18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Claims 2 and 4 have been cancelled by the applicant in amendment filed August 3, 2001.

Applicants' filing of substituted specification in Paper No. 9, received August 6, 2001 is acknowledged. However, there are still unclear and missing words on the top of these pages of substitute specification. A substitute specification including the claims for pages 1-32 and pages containing original claims 7 and 16 are required pursuant to 37 CFR 1.125(a).

The outstanding rejection of claims 1-18 under 35 USC 112, 2nd paragraph in the previous office action mailed April 3, 2001 is removed in view of the amendment filed August 6, 2001.

Applicants are merely requested to note however, that the terms "cellulose derivatives" in claim 11, 14, and "methacrylic derivatives and polyvinylpyrrolidone derivatives" in claim 14 are unclear in scope, due to the term "derivatives" as to compounds encompassed thereby. Although the specification lists several examples of the derivatives in page 6, line 14 - 19, it is not clear what further compounds may be encompassed by the instant claims.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the

invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 3, 5-18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Saunal et al. (WO96/30000, English equivalent: USPN 6,010,716 is also provided) and Winters et al. (WO95/30409) in view of Eibl et al. (USPN 5,290,769), Merck Index (Budavari et al., editor, Merck Index, 12th ed., 1996: page889-890, Compound 5232), and Remington's Pharmaceutical Sciences (Gennaro et al., Remington's Pharmaceutical Sciences, 18th ed., 1990: page 1305), all references of record in office action mailed April 3, 2001.

Saunal et al. teaches a transdermal topical formulation employing a solvent, absorption promoting agent, an active, comprising the steroid, nomegestrol, and a film-forming agent. Saunal et al. teaches the composition may contain 0.1 to 20.0% of nomegestrol (See col. 5, line 28). Saunal et al. also teaches the solvent or solubilizing agent may be ethanol or isopropanol(See col. 7, line 13). Sanual et al. also teaches that the weight ratio of the ethanol may be 44% to 84.9% (See particularly col. 7, line 41-46). The film-forming agent is a cellulose derivative, hydroxypropylmethylcellulose. (See col.3, line 58-59). The formulation of Saunal et al. also contains PVP VA, a known polyvinylpyrrolidone derivative (See col. 3, line 67).

Winters et al. teaches a topical formulation of the steroid, 19-nor progesterone for systemic delivery of active. The formulation has a solvent which may include alcohols (See page 4, line 1-2), film-forming agent such as methacrylates, and cellulose (See page 4, line 8-11), a plasticizing agent such as Labrasol (See page. 4, line 18), and a penetration enhancer.

The primary references do not expressly teach the use of the preferred carrier materials herein, propylene glycol, isopropylidene glycerol, isopropylideneglycerol, anionic copolymer of methacrylic acid and ethyl acrylate, and carbomer. The references do not expressly teach the weight ratio of nomegestrol to be 0.05 to 1%. The references do not expressly teach the ratio of water, ethanol, propylene glycol, and Labrasol in preferred solvent system herein.

However, Eibl et al. teaches the use of propylene glycol and copolymer of methacrylic acid and ethyl acrylate as pharmaceutical auxiliary agents in topical formulation (See col 5, line 66 and col. 6, line 19-20).

The Merck Index teaches that isopropylideneglycerol may be used as a solubilizing or plasticizing agent in pharmaceutical compositions (See page 889-890, Compound 5232).

Remington's Pharmaceutical Sciences teaches that carbomer is useful as a gelling and emulsifying agent in pharmaceutical compositions (See page 1305, col. 1).

Therefore it would have been obvious for one of ordinary skill in the art at the time the invention was made to formulate nomegestrol into a topical formulation with a gelling agent and other carrier materials herein in the amounts herein.

The employment of nomegestrol as an active agent in a topical pharmaceutical composition with carrier materials herein is motivated because these carrier materials are known pharmaceutical excipients, known to be useful in substantially similar topical pharmaceutical compositions comprising the same and similar active ingredients. The incorporation of known carrier materials into a pharmaceutical composition containing a

known active is considered within the skill of the artisan, absent evidence to the contrary.

The optimization of result effect parameters (e.g., amounts of ingredients) is obvious as being within the skill of the artisan, absent evidence to the contrary. Amounts of composition ingredients employed herein are substantially similar to the prior art. No unexpected result is seen hererin.

The instant composition containing nomegestrol would be reasonably expected to be similarly useful to raise progesterone levels in a host without regard to their status as being menopausal or premenopausal.

It is applicant's burden to demonstrate unexpected results over the closest prior art. See MPEP 716.02, also 716.02 (a) - (g). Furthermore, the unexpected results should be demonstrated with evidence that the differences in results are in fact unexpected and unobvious and of both statistical and practical significance. *Ex parte Gelles*, 22 USPQ2d 1318, 1319 (Bd. Pat. App. & Inter. 1992). Moreover, evidence as to any unexpected benefits must be "clear and convincing" *In re Lohr*, 137 USPQ 548 (CCPA 1963), and be of a scope reasonably commensurate with the scope of the subject matter claimed, *In re Linder*, 173 USPQ 356 (CCPA 1972). In regard to any possible unexpected result presented in the instant application, the data presented in examples I-III on pages 13-18 in the specification has been considered but not found persuasive as to the presence of an unexpected result over the prior art. In the instant case, the examples merely demonstrate and examine different formulations, using different concentrations of various ingredients, with respect to the solubility and the

penetration of the active, nomegestrol. The results are expected based on the cited prior art. No unexpected result is seen. Moreover, the clinical result of example IV demonstrates the effectiveness of the topical nomegestrol composition in delivering nomegestrol into the bloodstream. This is seen to be an expected effect based on the cited prior art. No comparative data to that of the prior art is demonstrated. No convincing and clear unexpected result is seen.

Response to Remarks

Applicant's remarks filed August 6, 2001 regarding the employment of impermissible hindsight reconstruction by the Examiner have been fully considered but they are not persuasive because the cited prior art clearly renders the claimed invention obvious as discussed in the previous office action and hereinabove. Please note that the broadest claim in the instant application, claim 1, only requires two components or ingredients, in the instant composition. The cited prior art teaches employment of both of ingredients a) and b) in claim 1 herein in a composition.

Applicant's remarks filed August 6, 2001 regarding the instant compositions not being for topical or transdermal use but for systemic use have been fully considered but not found persuasive because "intended use" does not lend patentable weight to claims drawn to compositions. See, e.g., *In re Hack* 114 USPQ 161. the cited prior art clearly renders obvious the employment of the active agent and carrier materials herein in a topical pharmaceutical composition.

Applicant's remarks filed August 6, 2001 regarding how drugs, especially nomegestrol diffuse through the dermal layer of the skin have been fully considered but

not found persuasive because all composition ingredients herein, including the active, nomegestrol, are known to be useful topical (or transdermal) pharmaceutical compositions.

Applicant's remarks filed August 6, 2001 regarding Saunal et al. not testing the specific examples containing 19-norprogesterone and therefore not teaching the instant composition have been considered but not found persuasive as to the non-obviousness of the instant invention because Saunal et al. clearly suggests that nomegestrol would be useful in the same composition although it does not expressly demonstrate examples employing nomegestrol. Obviousness does not require absolute predictability. See *In re Lamberti and Konort*, 192 USPQ 278 (CCPA 1976).

Applicant's assertion in the remarks filed August 6, 2001 that the instant invention is not to use a composition with known ingredients but to provide a specific pharmaceutical composition combining precise components for the beneficial use of systemic delivery of nomegestrol and/or its esters and ethers have been considered but not found persuasive because the broadest claim in the instant application, claim 1, only requires two components or ingredients, in the instant composition which are taught in the prior art. Further, nothing unobvious or unexpected over the prior is seen for the preferred solvent systems herein.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to San-ming Hui whose telephone number is (703) 305-1002. The examiner can normally be reached on Mon 9:00 to 1:00, Tu - Fri from 9:00 to 6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Minna Moezie, J.D., can be reached on (703) 308-4612. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4556 for regular communications and (703) 308-4556 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1235.

San-ming Hui
October 19, 2001

MINNA MOEZIE, J.D.
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600